

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Amended) A method of determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize ~~a thioamide or a thiocarbonyl~~ ethionamide, thiacetazone or thiocarlide, said method comprising detecting a mutation in an EtaA gene (SEQ ID NO:1) in said bacterium, which mutated gene encodes an amino acid sequence which differs from that of SEQ ID NO:2 by

(a) a frameshift mutation selected from the group consisting of: a deletion at position 65, an addition at position 567, and an addition at position 811, or

(b) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P, wherein detection of the mutation is indicative of decreased ability to oxidize ~~a thioamide or a thiocarbonyl~~ ethionamide, thiacetazone or thiocarlide.

2. (Canceled)

3. (Original) The method of claim 1, wherein the mutation is a single nucleotide polymorphism which causes an amino acid substitution in an amino acid sequence encoded by said EtaA gene compared to an amino acid sequence of SEQ ID NO:2.

4. (Canceled)

5. (Original) A method of claim 1 wherein the mutation is detected by
(a) amplifying the EtaA gene, or a portion thereof containing the mutation, with a set of primers to provide an amplified product,

(b) sequencing the amplified product to obtain a sequence, and

(c) comparing the sequence of the amplified product with the sequence of a wild-type EtaA gene (SEQ ID NO:1) or portion thereof,

wherein a difference between the sequence of the amplified product and the sequence of the wild-type EtaA gene or portion thereof indicates the presence of a mutation.

6-7. Canceled.

8. (Original) A method of claim 5, wherein said amplification is by polymerase chain reaction.

9. (Original) A method of claim 1, wherein said mutation is detected by hybridizing DNA from said bacterium to a test nucleic acid under stringent conditions.

10. (Original) A method of claim 9, wherein either said DNA from said bacterium or said test nucleic acid is immobilized on a solid support.

11. (Original) A method of claim 1, wherein said mutation is detected by
(a) subjecting said EtaA gene to digestion by restriction enzymes,
(b) separating the resulting restriction products to form a pattern of restriction fragment lengths, and

(c) comparing the pattern of restriction fragment lengths to a pattern of restriction fragment lengths formed by subjecting a known EtaA gene to the same restriction enzymes.

12. (Canceled)

13. (Withdrawn) A method of claim 1, wherein said mutation is detected by specifically binding an antibody to a mutated product of the EtaA gene, wherein the specific binding of the antibody to the mutated gene product is indicative of a mutation which inhibits the ability of the bacterium to oxidize a thioamide.

14. (Withdrawn) A method of claim 13, wherein said gene product is in, or is isolated from, sputum.

15. (Withdrawn) A method of claim 13, wherein detection of said specific binding of said antibody and said mutated gene product is by ELISA.

16. Canceled.

17. (Withdrawn) A method of claim 1, wherein said mutation is detected by
(a) culturing said bacterium in the presence of ethionamide; and
(b) testing for the presence or absence of (2-ethyl-pyridin-4-yl)methanol, wherein the absence of (2-ethyl-pyridin-4-yl)methanol indicates that the bacterium has a mutation which is indicative of decreased ability to oxidize a thioamide.

18 (Withdrawn) A method of claim 17 wherein the presence or absence of (2-ethyl-pyridin-4-yl)methanol is tested by subjecting a medium in which the bacterium is cultured, or the bacterium, to analysis by thin-layer chromatography, high pressure liquid chromatography, or mass spectrometry.

19 (Withdrawn) A method of claim 17, wherein the ethionamide of step (a) is radioactively labeled.

20. (Withdrawn) A method of claim 17, wherein the (2-ethyl-pyridin-4-yl)methanol is radioactively labeled.

21. (Currently amended) A method of screening an individual for a *Mycobacterium tuberculosis* bacterium resistant to treatment by ~~a thioamide or a thiocarbonyl~~ drug ethionamide, thiacetazone or thiocarlide, comprising

(a) obtaining a biological sample containing said bacterium from said individual,
and

(b) detecting a mutation in an EtaA gene (SEQ ID NO:1) in said bacterium, which

mutated gene encodes an amino acid sequence which differs from that of SEQ ID NO:2, wherein said mutation in said EtaA gene is selected from the group consisting of

(i) a frameshift mutation consisting of a deletion at position 65, an addition at position 567, or an addition at position 811, and

(ii) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P,

wherein detection of the mutation is indicative said bacterium is resistant to treatment by ~~a thioamide or a thiocarbonyl drug~~ ethionamide, thiacetazone or thiocarlide.

22. (Original) A method of claim 21, wherein the mutation is detected by

(a) amplifying the EtaA gene with a set of primers to provide an amplified product,

(b) sequencing the amplified product to obtain a sequence, and

(c) comparing the sequence of the amplified product with the sequence of a wild-type EtaA gene (SEQ ID NO:1),

wherein a difference between the sequence of the amplified product and the sequence of the wild-type EtaA gene indicates the presence of a mutation.

23-24. Canceled.

25. (Previously presented) A kit for determining the ability of a

Mycobacterium tuberculosis bacterium to oxidize ~~a thioamide or a thiocarbonyl~~ ethionamide, thiacetazone or thiocarlide, the kit comprising:

(a) a container, and

(b) primers for specifically amplifying an EtaA gene of said bacterium or a portion of said EtaA gene containing a mutation ~~affecting the ability of the bacterium to oxidize a thioamide~~ selected from the group consisting of (i) a frameshift mutation consisting of a deletion at position 65, an addition at position 567, or an addition at position 811, and

(ii) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P.

26-27. Canceled.

28. (Original) A kit of claim 25, further comprising a mutated EtaA gene for use as a positive control.

29. (Canceled)

30. (Withdrawn) A kit for determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide, the kit comprising:

- (a) a container, and
- (b) (2-ethyl-pyridin-4-yl)methanol.

31. (Withdrawn) A kit for determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide, the kit comprising:

- (a) a container, and
- (b) radiolabeled ethioamide.

32. (Withdrawn) A kit for determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide or thiocarbonyl, the kit comprising:

- (a) a container, and
- (b) an antibody which specifically binds to a product of a EtaA gene selected from the group consisting of a wild-type EtaA gene (SEQ ID NO:1) and a mutated EtaA gene.

33. (Withdrawn) A kit for determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide, the kit comprising:

- (a) a container, and
- (b) an antibody which specifically binds to (2-ethyl-pyridin-4-yl)methanol.

34. (Currently amended) A method of determining the ability of a *Mycobacterium tuberculosis* bacterium to oxidize a thioamide or a thiocarbonyl selected from the group consisting of ethionamide, thiacetazone and thiocarlide, said method comprising detecting a mutation in an EtaA gene (SEQ ID NO:1) in said bacterium, which mutated gene encodes an amino acid sequence which differs from that of SEQ ID NO:2, wherein said mutation is selected from the group consisting of

(a) a frameshift mutation consisting of a deletion at position 65, an addition at position 567, or an addition at position 811, and

(b) a single nucleotide polymorphism which causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P,

wherein detection of the mutation is indicative of decreased ability to oxidize ethionamide, thiacetazone or thiocarlide.

35. (Previously presented) The method of claim 34, wherein the mutation is a frameshift mutation selected from the group consisting of: a deletion at position 65, an addition at position 567, and an addition at position 811.

36. (Canceled)

37. (Currently amended) The method of claim ~~36~~ 34, wherein the single nucleotide polymorphism causes an amino acid substitution selected from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P.

38. (Previously presented) A method of claim 34 wherein the mutation is detected by

(a) amplifying the EtaA gene, or a portion thereof containing the mutation, with a set of primers to provide an amplified product,

(b) sequencing the amplified product to obtain a sequence, and

(c) comparing the sequence of the amplified product with the sequence of a wild-type EtaA gene (SEQ ID NO:1) or portion thereof,

wherein a difference between the sequence of the amplified product and the sequence of the wild-type EtaA gene or portion thereof indicates the presence of a mutation.

39. (Previously presented) A method of claim 38, wherein said amplification is by polymerase chain reaction.

40. (Previously presented) A method of claim 34, wherein said mutation is detected by hybridizing DNA from said bacterium to a test nucleic acid under stringent conditions.

41. (Previously presented) A method of claim 40, wherein either said DNA from said bacterium or said test nucleic acid is immobilized on a solid support.

42. (Previously presented) A method of claim 34, wherein said mutation is detected by

(a) subjecting said EtaA gene to digestion by restriction enzymes,

(b) separating the resulting restriction products to form a pattern of restriction fragment lengths, and

(c) comparing the pattern of restriction fragment lengths to a pattern of restriction fragment lengths formed by subjecting a known EtaA gene to the same restriction enzymes.

43. (Canceled)

44. (Currently amended) A method of screening an individual for a *Mycobacterium tuberculosis* bacterium resistant to treatment by a thioamide or a thiocarbonyl drug, selected from the group consisting of ethionamide, thiacetazone and thiocarlide, comprising

(a) obtaining a biological sample containing said bacterium from said individual,
and

(b) detecting a mutation in an EtaA gene (SEQ ID NO:1) in said bacterium,
wherein said mutation is selected from the group consisting of (a) a frameshift mutation
consisting of a deletion at position 65, an addition at position 567, and an addition at position
811, and (b) a single nucleotide polymorphism which causes an amino acid substitution selected
from the group consisting of: G43C, P51L, D58A, Y84D, T186K, T342K, and A381P, wherein
detection of the mutation is indicative said bacterium is resistant to treatment by ethionamide,
thiacetazone or thiocarlide.

45. (Previously presented) A method of claim 44, wherein the mutation is
detected by

(a) amplifying the EtaA gene with a set of primers to provide an amplified
product,

(b) sequencing the amplified product to obtain a sequence, and

(c) comparing the sequence of the amplified product with the sequence of
a wild-type EtaA gene (SEQ ID NO:1),

wherein a difference between the sequence of the amplified product and the
sequence of the wild-type EtaA gene indicates the presence of a mutation.

46. (Previously presented) A kit for determining the ability of a
Mycobacterium tuberculosis bacterium to oxidize a thioamide or a thiocarbonyl selected from
the group consisting of ethionamide, thiacetazone and thiocarlide, the kit comprising:

(a) a container, and

(b) primers specific for amplifying an EtaA gene of said bacterium or a portion of
said EtaA gene containing a mutation affecting the ability of the bacterium to oxidize
ethionamide, thiacetazone or thiocarlide